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Validation of the Hamilton Rating Scale for Depression in adults with epilepsy

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ABSTRACT

Purpose: Mood disorders represent a frequent psychiatric comorbidity among patients with epilepsy, having a major impact on their quality of life and contributing considerably to the global burden of the disease. The availability of standardized clinical instruments validated in populations with epilepsy has important implications in terms of diagnosis and treatment. This aimed to validate the Hamilton Rating Scale for Depression (HRSD) in adult patients with epilepsy.
Methods: A consecutive sample of 120 adult outpatients with epilepsy was assessed using the Mini International Neuropsychiatric Inventory (MINI) Plus version 5.0.0 and the HRSD.
Results: Cronbach's alpha coefficient was 0.824 for the 17-item version and 0.833 for the 21-item version. Receiver operating characteristic analysis showed an area under the curve of 0.896 and 0.899, respectively, for the two versions. However, the HRSD-17 demonstrated the best psychometric properties compared to the HRSD-21 and, with a cutoff score of 6, showed a sensitivity of 94%, a specificity of 80%, a positive predictive value of 46%, and a negative predictive value of 99%.
Conclusions: The HRSD proved to be reliable and valid in the epilepsy setting and will stimulate further research in this area.

1. Introduction

Depression is the most frequently reported psychiatric comorbidity in epilepsy, with lifetime prevalence rates ranging between 24% in community-based studies [1] and 50% in tertiary referral centers or surgery programs [2,3]. Reasons for such a close link are both biological and psychosocial. In fact, on the one hand, epilepsy is a chronic disorder which brings about social discriminations and everyday life limitations [4]. On the other hand, neuroimaging and neurobiological studies are emphasizing the biological contribution to this association based on neuroanatomical and neurochemical principles [5,6]. This is further supported by epidemiological studies suggesting a bidirectional relationship between the two disorders, meaning that depression does not always follow the onset of the epilepsy but it may also precede a seizure disorder [7,8], suggesting an underlying common neurobiological background [6].

One of the most frequent methodological errors in research studies on depression in epilepsy is the use of measures or cutoff scores that may not be valid in populations with epilepsy [9]. At the moment, we have a limited number of clinical instruments for depression validated in the epilepsy setting, namely the Neurological Disorder Depression Inventory for Epilepsy (NDDIE) [10] and the Beck Depression Inventory (BDI) [11]. The former has been developed to screen patients for a current depressive episode, while the latter is a well-known self-report inventory for depressive symptoms. The BDI suffers from the same problems as other self-report inventories, namely that scores can be easily exaggerated or minimized by the person completing them. The Hamilton Rating Scale for Depression (HRSD) has represented the gold standard for the assessment of depression for more than 40 years [12]. It is a measure of severity of depressive symptoms rated by a clinician. It explores main biological symptoms of depression such as low mood, insomnia, agitation, anxiety, and weight loss. Initially developed in the late 1950s to assess the effectiveness of the first generation of antidepressants, the HRSD has retained its function and is now the most commonly used measure of depression in clinical and research practice in psychiatry. In fact, it is widely available around the world, having been translated in a number of different languages.

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This study aimed to validate the psychometric properties of the HRSD in patients with epilepsy in order to identify its specificity, sensitivity, and cutoff scores.

2. Methods

2.1. Study sample

A consecutive sample of adult outpatients with epilepsy was invited to participate in the study. To be enrolled, patients had to fulfill the following criteria: (1) diagnosis of epilepsy according to the ILAE criteria, (2) age of more than 18 years, (3) absence of severe medical diseases, and (4) willingness to provide written informed consent to undergo the experimental procedures. Patients provided written informed consent after receiving a complete description of the study and having an opportunity to ask questions.

2.2. Instruments

All subjects were assessed using the MINI Plus version 5.0.0 [13] and the HRSD [14], Italian versions [15].

The MINI Plus 5.0.0 is an efficient diagnostic interview following DSM criteria. It screens for a number of axis I diagnoses with brief suicidality and antisocial personality modules. It has been validated in the United States and Europe and is available in several languages. Moreover, it has been validated in the epilepsy setting [16], and it is widely accepted as a gold standard for clinical research in this area.

In the HRSD, the clinician has to choose the possible response to each question by interviewing the patient and by observing the patient's behavior. Each question has between 3 and 5 possible responses that increase in severity. In the original scale published in 1960, the first 17 questions contribute to the total score (HRSD-17). Administration time is about 20–30 min. A score of 0–7 is considered to be normal; scores of 20 or higher indicate moderately severe depression and are usually required for entry into a clinical trial. Questions 18–21 may be recorded to give further information about the depression (such as whether diurnal variation or paranoid symptoms are present) but are not part of the scale. Factor analyses in patients with mood disorders of the HRSD identified six factors: anxiety/somatic symptoms, weight changes, cognitive symptoms, rhythmicity, psychomotor retardation, and sleep [17].

Both instruments, the MINI and the HRSD, were administered in a standardized way and in the same sequence in all patients.

2.3. Experimental procedures and statistical analyses

The MINI was used as the gold standard for the diagnosis of current major depression. Both versions of the HRSD (17 and 21 items) were tested. The HRSD factors have been tested as they have been identified, without separate factor analyses in patients with epilepsy, because such factors are widely used in the current psychiatric literature.

When validating a psychometric instrument, it is important to evaluate reliability and validity [18]. Reliability has been tested by investigating internal consistency that explores whether items that propose to measure the same general construct produce similar scores [18]. Validity has been investigated by measuring concurrent validity that represents the degree to which a measure is correlated with other measures of the same construct [18]. Cronbach's coefficient was used to test internal consistency. The MINI was used to test concurrent validity, and a ROC analysis was computed to establish specificity, sensitivity, and positive and negative predictive values. Sensitivity measures the proportion of actual positives that are correctly identified as such, while specificity measures the proportion of negatives that are correctly identified as such. The positive and negative predictive values (PPV and NPV, respectively) are the proportions of positive and negative results that are true positive and true negative results and describe the performance of a diagnostic test [18].

Frequencies of categorical, demographic, and clinical variables were analyzed using the χ^2 analysis or Fisher's exact test. Continuous demographic and clinical variables and HRSD scores were compared using the Mann–Whitney test. Analyses were carried out using SPSS version 15.0 for Windows.

Table 1
Clinical and demographic features of the study sample.

	N = 120 (%)
Age, mean ± SD	44.9 ± 14.4
Gender	
Male	60 (50)
Female	60 (50)
Age at onset of epilepsy, mean ± SD	26.0 ± 18.4
Epilepsy type	
Focal	90 (75)
Generalized	30 (25)
Brain MRI normal	63 (52.5)
Therapy	
None	6 (5)
Monotherapy	71 (59.2)
Dualtherapy	30 (25)
Polytherapy	13(10.8)

3. Results

A total of 120 outpatients with epilepsy participated in the study. Clinical and demographic characteristics are shown in Table 1. According to the MINI, a diagnosis of major depression (current episode) was established in 29 (24.2%) patients. Mean HRSD total and factor scores in depressed and nondepressed patients are shown in Table 2.

Cronbach's alpha was 0.824 for the HRSD-17 and 0.833 for the HRSD-21. Receiver operating characteristic analyses for the HRSD and its factors are shown in Table 3. The HRSD-17 demonstrated the best psychometric properties and, with a cutoff score of 6, showed a sensitivity of 94%, a specificity of 80% (Fig. 1), a positive predictive value of 46%, and a negative predictive value of 99% (Table 4).

4. Discussion

Major depression represents a frequent psychiatric comorbidity that negatively affects mortality and morbidity [4,19]. However, it frequently goes unrecognized and untreated and the lack of standardized clinical instruments is one of the reasons. The HRSD showed more than acceptable psychometric properties in patients with epilepsy with a good internal consistency. Our study identified a slightly different cutoff score than that usually adopted in the general population, namely six instead of eight. Although it may be argued that this can be partially explained by the small sample size, it further suggests the need for identifying cutoff scores validated in populations with epilepsy rather than adopting those reported in the general population. As stated at the beginning,

Table 2
Hamilton Rating Scale for Depression (HRSD) mean total and factor scores in depressed and nondepressed patients.

	Depressed (29)	Nondepressed (91)	Mann–Whitney Z	P value
HRSD-21	13.0 ± 4.7	3.9 ± 5.2	5.450	<0.001
HRSD-17	11.5 ± 4.5	3.6 ± 4.7	5.423	<0.001
Anxiety/somatic	3.9 ± 2.2	1.3 ± 1.8	4.565	<0.001
Weight	0.6 ± 1.1	0.3 ± 1.1	2.476	0.013
Cognition	2.5 ± 2.1	0.7 ± 1.5	4.499	<0.001
Rhythmicity	0.9 ± 1.1	0.2 ± 0.6	3.463	0.001
Psychomotor retardation	2.6 ± 1.5	0.6 ± 1.1	5.185	<0.001
Sleep	1.2 ± 1.0	0.4 ± 0.8	3.719	<0.001